

IN THE SPECIFICATION:

Please replace the paragraph beginning at line 1 of page 4 with the following rewritten paragraph:

- - The unavailability of any simple laboratory test to classify GI bleeding as an upper or lower GI bleed is a problem that is well-understood ~~problem~~ by nearly all clinicians. It is not surprising then that while evaluating a new and highly sensitive fluorometric test (HemoQuant™) for occult blood, the need for such a test prompted Schwartz et al to publish an article suggesting further study of the HemoQuant™ test as a possible means of distinguishing bleeding sites. See Schwartz S, Dahl J, Ellefson M, Ahlquist D., "The HemoQuant test: A specific and quantitative determination of heme (hemoglobin) in feces and other materials", Clin. Chem. 1985;29:2061-2067. The HemoQuant™ test involves the conversion of heme into dicarboxylic porphyrins (e.g. hematoporphyrin). Heme is a core, non-protein part of hemoglobin that binds iron, and provides much of the material which is visible to spectroscopy. The dicarboxylic porphyrins absorb strongly at 402 nanometers and fluoresce at 653 nanometers. This provides a quantitative and sensitive measure of the hemoglobin present. As discussed above, hemoglobin in the intestines is exposed to a large population of bacteria, which can also degrade hemoglobin to dicarboxylic porphyrins. These products may be measured separately and are called the intestinal converted fraction (ICF). It was postulated that the more proximal the bleeding site the longer the exposure to bacteria and the greater the ICF. Indeed, this was subsequently noted to be the general trend. See Ahlquist DA, McGill DB, Schwartz S, Taylor SF, et al., "Fecal blood levels in health and disease: A study using HemoQuant", N. Engl. J.

Med. 1985. 312:1422-1428. However, after studying a large sample of patients it was found that while the ICF appeared to be affected by the site and amount of bleeding (for example the mean ICF was significantly lower in patients with bleeding from sigmoid or rectal lesions compared to more proximal lesions) it was concluded that the considerable individual differences in enteric heme metabolism severely compromised the predictive value of the ICF . See Goldschmidt MD, Ahlquist DA, Wieand HS, McGill DB, et. al., "Measurement of degraded fecal hemoglobin-heme to estimate gastrointestinal site of occult bleeding: appraisal of its clinical utility", Digestive Diseases and Sciences, 1988, 33:605-608. Consequently, the ICF was thought to be of no clinical utility in estimating the bleeding site.- -

Please replace the paragraph beginning at line 4 of page 8 with the following rewritten paragraph:

- - Briefly described, and in accordance with one embodiment thereof, the invention provides a means for determining with a high degree of certainty whether blood in a patients' stool originated from a bleeding site in the duodenum or above or a bleeding site in the colon or small intestine. A stool specimen from a patient that has been determined to be bleeding in the gastrointestinal tract is placed directly into a tube containing a hypotonic buffer. The stool specimen is delivered to a doctor (or other health-care professional) who centrifuges the specimen to remove particulate matter. A portion of the supernatant is then filtered through a small nitrocellulose filter. In the described embodiment, the filter is then wetted with a 60% glycerol buffer solution, which increases the translucency of the filter. The filter is then placed in a spectrophotometer, which determines an absorbance curve for the filter relative to a blank

filter that does not have a specimen on it. The absorbance curve is analyzed by a computer program to determine whether the bleeding is from the upper or lower gastrointestinal tract, on the basis of the relative amounts of ferric and ferrous heme present in the sample, and the computer displays information indicating whether the bleeding is from the upper or lower gastrointestinal tract. A sample with significant amounts of ferric heme would be considered to represent a likely upper gastrointestinal bleed. A sample with significant amounts of ferroheme would be considered a probable lower gastrointestinal bleed. The physician would then tailor the treatment of the patient with this information. For example, if the test indicates an upper GI bleed, the physician may give the patient a trial with an H2 blocker and follow the patient's progress, saving \$1,000 of resource utilization (i.e. colonoscopy procedure and work-up). If the test indicates a lower GI bleed, then the patient would need to be further evaluated, for example by colonoscopy, because of the risk of colorectal cancer.- -

Please replace the paragraph beginning at line 10 of page 14 with the following rewritten paragraph:

- - These changes that occur to hemoglobin molecules that have originated from an upper GI bleed and therefore have passed through the acidic environment of the stomach are indicated by the absorption characteristic shown in Fig. 2. Specifically, the two main absorption peaks labeled α and β around 540 nanometers and 576 nanometers, respectively, for "normal hemoglobin" molecules are eliminated from "acid-treated hemoglobin" molecules that have passed through the stomach. Also, there is a shift in the absorption peak of the main Soret band (from about 415 nanometers to 408 nanometers) between the absorption characteristic of normal

hemoglobin molecules and "acid treated" hemoglobin molecules. There is also a reduction in the molar extinction coefficient for the Soret band. The absorption pattern is due to the heme component, as digestion with trypsin or proteinase K (as might occur in the GI tract) does not significantly alter the absorption spectra. - -

Please replace the paragraph beginning at line 9 of page 16 with the following rewritten paragraph:

- - The ability of this technique to detect hemoglobin in the stool can be tested by mixing a small amount of blood ($2\ \mu\text{l}$) with a stool sample (40 mg). It should be noted that the normal level of blood loss is about $0.5\ \mu\text{l}$ of blood per 40 mg stool, while a level of about $7\ \mu\text{l}$ of blood per 40 mg stool is considered to be a positive occult bleed. See Wallach J. "Interpretation of Diagnostic Tests", Little, Brown and Company (Boston). 1992. p. 154. The sample was extracted and the spectrum of the supernatant before and after binding to the translucent membrane is compared in Fig. 4. This result shows the expected benefit in signal to background noise that can be obtained. In fact, the hemoglobin absorption peaks in curves A and B at 540 and 576 nanometers, respectively, can be clearly detected in the membrane bound sample, but are completely obscured in solution. These peaks are important in producing a high specificity test. - -

Please replace the paragraph beginning at line 14 of page 19 with the following rewritten paragraph:

- - The reference filter cup 8 is placed into a visible spectrophotometer and the transmission of the light from the light source through the nitrocellulose filter 9 is adjusted to provide a maximum reading that is still in the measurable range. The reference filter cup 8 is then removed from the spectrophotometer and replaced with the sample filter cup 4. The characteristic of the transmission of light through nitrocellulose filter 6 is then determined and compared to that of the nitrocellulose filter 9 which determines the sample absorbance spectrum of the material bound to and hence concentrated on the nitrocellulose filter 6 over the wavelength ranges of 400 to 600 nanometers, as shown by curve B in Fig. 4. The sample absorbance spectrum is analyzed by means of an artificial neural net, such as Neuroshell Classifier®, available from Ward Systems Group, Inc., Frederick, MD (the main character), running on a conventional personal computer. The neural net, which has been trained with multiple spectra of normal and acid-treated hemoglobin mixed with stool samples, classifies the sample spectrum as a result of either upper gastrointestinal bleeding, lower gastrointestinal bleeding or no blood present. - -

Please replace the paragraph beginning, in the Abstract of the Disclosure, at line 2 of page 36 with the following rewritten paragraph:

- - A method for determining if blood in a stool sample originated from the upper or lower gastrointestinal tract. This includes a method for purifying and concentrating hemoglobin and its ~~its~~² products from a stool sample to allow a simple and sensitive spectrophotometric analysis. A rapid, noninvasive determination of whether the blood originated from an upper gastrointestinal or lower gastrointestinal site is made on the basis of changes in the absorption

spectra of hemoglobin that occur when hemoglobin is exposed to a highly acidic environment. - -